REMARKS/ARGUMENTS

Responsive to the Office Action dated January 28, 2008, Claims 1 and 11 have been amended. Claims 1-20 remain pending for prosecution with Claims 1 and 11 being independent. Declarations under 37 C.F.R. 1.132 executed by inventors of the present invention, Dr. Benjamin P. Warner (hereinafter "Warner") and Dr. George J. Havrilla (hereinafter "Havrilla"), were previously submitted.

I. Improper Rejections

Applicant acknowledges with appreciation the withdrawal of the rejection of Claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over Pirrung et al. in view of Wang. However, Applicant respectfully submits that the new Examiner's statement in the instant Office Action that "Applicant's arguments with respect to Claims 1-20 have been considered but are moot in view of the new ground(s) of rejection" and failure to address Applicant's previously-submitted arguments against the obviousness rejection are improper and evidence of a piecemeal examination. The Examiner is required to answer all material traversed and make clear statements as to the withdrawal of rejections and the reasons why the rejections are being withdrawn. The Examiner has not complied with any of these rules.

Furthermore, Applicant submits that the new grounds of rejection are improper in that Applicant made no amendments to the claims in its last response. Moreover, full faith and credit should be given to the search and action of a previous examiner unless there is a clear error in the previous action or knowledge of other prior art. In general, an examiner should not take an entirely new approach or attempt to reorient the point of view of a previous examiner, or make a new search in the mere hope of finding something. Amgen, Inc. v. Hoechst Marion Roussel, Inc.,

126 F. Supp. 2d 69, 139, 57 USPQ2d 1449, 1499-50 (D. Mass. 2001). Applicant therefore respectfully submits that there was no need for a new search of the prior art to be conducted and requests withdrawal of these improper rejections.

II. Claim Rejections - 35 U.S.C. § 112

A. Rejection of Claims 1-10

Claims 1-10 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, it was asserted that the amendments to Claim 1 made in Applicant's January 19, 2007 Reply were not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In view of the Examiner's comments, Applicant has amended Claim 1 in order to clarify that the X-ray fluorescence signal is generated by a detectable element present in the binder and, thus, a bound receptor. Applicant therefore respectfully requests reconsideration and withdrawal of this rejection.

B. Rejection of Claims 1-20

Claims 1-20 were rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. In particular, it was asserted that the missing steps are "a separation or wash step." Applicant has amended independent Claims 1 and 11 to include a separation step and therefore respectfully requests reconsideration and withdrawal of this rejection.

C. Rejection of Claims 11-20

Claims 11-20 were also rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. In particular, it was asserted that the omitted element is that the untagged binder contains an element capable of producing X-ray fluorescence. Applicant has amended independent Claim 11 to include this element and therefore respectfully requests reconsideration and withdrawal of this rejection.

III. Claim Rejections - 35 U.S.C. § 102

A. Rejection of Claims 1-8, 10-18, and 20 over Wang

Claims 1-8, 10-18 and 20 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 4,663,277 to Wang in light of U.S. Patent No. 4,830,192 to Plester. For the following reasons, Applicant respectfully requests reconsideration and withdrawal of this rejection.

The Office Action asserts that Wang teaches "methods for detecting viruses and/or proteins, in which a plurality of viruses or proteins (i.e., receptors) in a specimen is exposed to an extended solid phase component (i.e., substrate) which is coated in at least one location with antiviral or antiprotein antibody." It is asserted that "[t]his step in which viruses in the sample are bound to the solid phase via the antiviral or antiprotein antibodies reads on the claimed step of 'arraying' the receptors on a substrate when given its broadest reasonable interpretation." Moreover, the Office Action asserts that Wang teaches "exposing the arrayed receptors to at least one potential binder, namely the same antibody coated onto a mobile solid phase of dispersed microspheres." "In one embodiment, the microspheres in the binder may be doped with metal elements so as to enable detection by X-ray fluorescence . . ." and "[d]etection of the X-ray

fluorescence of the metal element labels in the microspheres indicates that binding between the receptors and the solid phased antibody(ies) has occurred."

It is also noted that Wang teaches X-ray fluorescence detection, but does not specifically disclose whether this process involved irradiation with X-rays to produce the fluorescence signal. Plester et al. is therefore cited as evidence that X-ray fluorescence involves the excitation of a sample by irradiation of the material with X-rays. Therefore, it is asserted that "the teachings of Wang read on the instantly claimed step of exposing the array members to X-ray radiation."

Further, the Office Action states that "[a]lthough the methods of Wang involve first arraying the receptors on the extended solid phase, followed by contacting with the plurality of antibody-microsphere binders, it is noted that the instant claims do not require any particular order in which steps (a) and (b) of claims 1 and 11 are performed."

Applicant respectfully traverses these assertions and respectfully submits that Wang does not anticipate the present invention because Wang fails to disclose each and every element of the invention as claimed. In particular, and as acknowledged by the Office Action itself, Wang involves *first* arraying the receptors on the extended solid phase *followed by* contacting with the plurality of antibody-microsphere binders. The claimed invention, on the other hand, requires that the unbound receptors be exposed to the binders prior to being arrayed onto a substrate. It is asserted in the Office Action that "the instant claims do not require any particular order in which steps (a) and (b) of claims 1 and 11 are performed." However, as a matter of logic, the language of the method claims at issue do require step (a) to be performed before step (b). The specification, directly and impliedly, also imposes this order on the method steps. Applicant therefore submits that Wang fails to disclose the exposing step followed by the arraying step as claimed by Applicant in independent Claims 1 and 11.

It is also asserted in the Office Action that, with regard to the instantly claimed "untagged" binder, the "instant specification defines a 'tagged' ligand as one that is 'attached via one or more chemical bonds to a chemical portion that fluorescences [sic] when exposed to non-ionizing, ultraviolet radiation' (page 2, lines 27-30)." Therefore, the Examiner states that "an 'untagged' potential binder would be one that is not fluorescently tagged." Moreover, it is asserted that "[s]ince there is nothing in this definition that would rule out attachment of moieties that fluorescence [sic] when exposed to *ionizing* radiation (i.e., X-rays)." Therefore, the Examiner concludes that "when the claims are given their broadest reasonable interpretation, the antibody-microsphere binders of Wang may be considered 'untagged' according to Applicant's definition since they do not contain tags that fluorescence [sic] when exposed to nonionizing, UV radiation, but rather contain metal elements that fluorescence [sic] when exposed to ionizing X-rays (as in the instant specification)."

Applicant respectfully traverses the Examiner's interpretation of the term "untagged." It is well known in the art that tagging involves modifying the original chemical by attaching a "tag" (a chemical group that fluoresces when exposed to ultraviolet or visible light, for example) to all or a portion of the chemical. The Examiner has unnecessarily limited the definition of "untagged" to one example used in describing a particular reference. It is clear from the context of the present application and the general knowledge of those skilled in the art that the term "untagged" means elements that are chemically associated and that are intrinsically integral to the component being measured. In the present application, Applicant's method requires exposing an unbound receptor to a binder that includes an element detectable by X-ray fluorescence to form at least one bound receptor as claimed in Claim 1 and Claim 11 requires that the binder be untagged. Wang, on the other hand, does not teach the detection of X-ray

fluorescence from a bound receptor-binder complex. Wang also does not teach the detection of X-ray fluorescence directly from a binder. Rather, Wang detects X-ray fluorescence from a tag. In other words, without the required tag, Wang would not be able to detect any X-ray fluorescence from the array or the binder. *See previously submitted Declarations by Warner ¶ 8(ii) and Havrilla ¶ 8(ii).* This fact is further evidenced by the requirement that Wang's "microspheres can include dye or fluorescent compounds for direct visual observation, or have metal elements or iron oxide doped or entrapped within in order to provide X-ray fluorescent or electromagnetic signals." Moreover, in order for the tags to remain chemically unassociated, Wang encloses the tag in latex or a similar coating. In contrast, Applicant's claimed invention measures elements that are chemically associated and that are intrinsically integral to the component being measured since it is the bound array members that are being detected by X-ray fluorescence and not a "chemically unassociated" tag or label. *See Warner ¶ 8(iii) and Havrilla ¶ 8(iii).*

In fact, Wang is nothing more than a part of the background for one of the unsolved needs in the art met by the present invention. As stated in Applicant's Background of the Invention, the attachment of a fluorescent tag to a chemical or receptor could result in a conformational change which has been known to affect the binding affinity of the chemical or receptor because the tagged surrogates are structurally different from their untagged counterparts. The present invention is therefore concerned with the evaluating the binding properties of receptors and chemicals using the untagged chemical or receptor and not with a tagged surrogate as disclosed by Wang.

Therefore, because Wang fails to disclose each and every element of Applicant's independent Claims 1 and 11 and the claims depending therefrom, Wang does not anticipate the present invention. Applicant therefore respectfully requests withdrawal of this rejection.

B. Rejection of Claims 1-5, 9-15, and 19-20 over Sano

Claims 1-5, 9-15 and 19-20 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,391,590 to Sano et al. in light of U.S. Patent No. 4,830,192 to Plester. For the following reasons, Applicant respectfully requests reconsideration and withdrawal of this rejection.

The Office Action asserts that "Sano et al. teach methods of determining metal-binding activity of streptavidin-metallothionein chimeric protein, in which the receptors (i.e., chimeric proteins) are exposed to at least one potential binder, namely, the metal ion Cd^{2+} which is provided as $CdCl_2$ during the course of protein purification." It is then asserted that "[t]he reference further teaches spotting (i.e. arraying) the proteins onto a substrate (polypropylene membrane)." "The arrayed proteins were then subjected to quantitative X-ray fluorescence in order to determine the amount of metals in the sample spot." Plester is cited as evidence "that X-ray fluorescence involves the excitation of sample by irradiation of the material with X-rays."

Applicant respectfully traverses the Office Action's assertions of anticipation and respectfully submits that Sano fails to anticipate the present invention because Sano does not disclose each and every limitation of the claims at issue. In the present application, Applicant's method requires exposing an unbound receptor to a binder that includes an element detectable by X-ray fluorescence to form at least one bound receptor as claimed in Claim 1 and Claim 11 requires that the binder be untagged. Sano, on the other hand, does not teach the detection of X-ray fluorescence from a bound receptor-binder complex. Sano also does not teach the detection

of X-ray fluorescence directly from a binder. Rather, Sano detects X-ray fluorescence from a tag. In other words, without the required tag, Sano would not be able to detect any X-ray fluorescence from the array or the binder. *See Warner ¶ 8(ii) and Havrilla ¶ 8(ii).* The Office Action itself supports this conclusion because "the metal ion Cd^{2+} which is provided as $CdCl_2$ during the course of protein purification" cited by the Office Action is, in fact, a radioactive label or tag. In contrast, Applicant's claimed invention measures elements that are chemically associated and that are intrinsically integral to the component being measured since it is the bound array members that are being detected by X-ray fluorescence and not a "chemically unassociated" tag or label. *See Warner ¶ 8(iii) and Havrilla ¶ 8(iii).*

Sano is therefore nothing more than a part of the background for one of the unsolved needs in the art met by the present invention. As stated in Applicant's Background of the Invention, the attachment of a fluorescent tag to a chemical or receptor could result in a conformational change which has been known to affect the binding affinity of the chemical or receptor because the tagged surrogates are structurally different from their untagged counterparts. The present invention is therefore concerned with the evaluating the binding properties of receptors and chemicals using the untagged chemical or receptor and not with a tagged surrogate as disclosed by Sano.

Therefore, because Sano fails to disclose each and every element of Applicant's independent Claims 1 and 11 and the claims depending therefrom, Sano does not anticipate the present invention. Applicant therefore respectfully requests withdrawal of this rejection.

IV. Double Patenting Rejections

Claims 1-20 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-42 of copending Application No. 10/880,388 and claims 1-19 of copending Application No. 11/974,156. Applicant respectfully submits that the currently pending claims of the present application, as amended, are patentably distinct from Application No. 10/880,388 and Application No. 11/974,156. Applicant therefore respectfully requests reconsideration and withdrawal of this rejection.

V. Conclusion

Applicant respectfully submits the claims are in condition for formal allowance and such is courteously solicited. If any issue regarding the allowability of any of the pending claims in the present application could be readily resolved, or if other action could be taken to further advance this application such as an Examiner's amendment, or if the Examiner should have any questions regarding the present amendment, it is respectfully requested that the Examiner please telephone Applicant's undersigned attorney in this regard. Should any fees be necessitated by this response, the Commissioner is hereby authorized to deduct such fees from Deposit Account No. 11-0160.

Respectfully submitted,

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